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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,964	09/08/2000	Meir Shinitzky	24259	9351

7590 02/28/2005

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,964	SHINITZKY ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/04 has been entered.

2. Claims 6-13 are pending and are being acted upon in this Office Action.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite because the method is incomplete, merely preparing a protein fraction from platelet will not achieve the goal of "detecting a DTH reaction in said individual"; the method steps of injecting the platelet preparation into a subject and detecting occurrence of a delayed type hypersensitivity reaction at the site of injection must be added. Further, the claim should culminate in a phrase such as "wherein a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic."

The "...pI of said proteins or fractions thereof is greater than about 6.5" in claims 6, 7, 8, and 9 is indefinite because the term "greater than" renders the upper limits of the pI to infinity. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 7-9 are rejected under 35 U.S.C. 102(b) or in the alternative 102(a) as being anticipated by Deckmann et al (Ital. J Psych Behav Sci 6: 29-34, 1996; PTO 892).

Deckmann et al teach a diagnostic method for determining schizophrenia in a subject such as non schizophrenic (control) and patient with schizophrenia comprising obtaining a preparation comprising platelet derived proteins from self, injecting said preparation into a subject and examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of injection and positive reaction at the site of injection indicating that the subject has a high likelihood of being schizophrenic (see Table 2, page 33, col. 1, in particular), The reference platelet derived proteins inherently have a pI greater than about 6.5 since the claimed platelet fraction does not have a particular molecular weight. Deckmann et al skin test with platelet provides a basis for the biochemical diagnosis of schizophrenia (see page 29, col. 1, in particular). Thus, the reference teachings anticipate the claimed invention.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deckmann et al (Ital. J Psych Behav Sci 6: 29-34, 1996; PTO 892) in view of WO 97/13152 publication (or record, April 1997; PTO 1449) and Rotman *et al* (Prog Neuropsychopharmacol Biol Psychiatry 7(2-3): 135-41, 1983; PTO 1449).

The teachings of Deckmann et al have been discussed supra.

The claimed invention in claim 6 differs from the teachings of the reference only in that a method for preparing a reagent for use in diagnosis of schizophrenia in an individual by detecting a DTH reaction in said individual following injection of said reagent to the individual, comprising: a) obtaining blood samples from a number of individuals, preparing a pool from said samples and collecting platelets therefrom; b) preparing a protein fraction from said platelet preparation comprising proteins or fractions thereof, wherein the pl of said proteins or fractions thereof is greater than about 6.5.

The claimed invention in claims 10-13 differs from the teachings of the reference only in that a diagnostic method for determining schizophrenia wherein the protein is platelet derived proteins or fractions thereof having a pI within the range of about 6.5 to about 9.5 instead of neurospecific proteins S-100 and 10-40-4.

The WO 97/13152 publication teaches a method for preparing a reagent for diagnosis of mental disorder such as dementia comprising the steps of obtaining blood from a number of individuals or individual such as demented patients or healthy normal subjects, isolating platelet from the said blood samples (See entire document, page 8 in particular), preparing protein fractions from the reference platelet preparation having a pI between 7 and 9, which is *greater than about* 6.5 (See page 12, Fig 4, page 10, Preparative isoelectric focusing, in particular). The reference pI is also within the claimed range of above 6.5 to about 9.5 (see page 12, lines 20-21, Fig. 4, in particular).

Rotman *et al* teach blood platelets are a very good model for nerve endings, serotonin uptake and imipramine binding and the efficiency of various drugs such as antidepressants have been evaluated using blood platelets instead of synaptosomes (See abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare platelet protein having a pI between 7 and 9, which is *greater than about* 6.5 or within the range of above 6.5 to about 9.5 as taught by WO 97/13152 publication for use in diagnosis of schizophrenia as taught by Deckmann et al. From the combined teachings of

the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Deckmann et al skin test with platelet provides a basis for the biochemical diagnosis of schizophrenia (see page 29, col. 1, in particular). Rotman *et al* teach blood platelets are a very good model for nerve endings, serotonin uptake and imipramine binding and the efficiency of various drugs such as antidepressants have been evaluated using blood platelets instead of synaptosomes (See abstract, in particular). Platelet preparation having a pI between 7 and 9 can be easily prepared by the method as taught by the WO 97/13152 publication for various neurological disorders (See page 12, Fig 4, page 10, Preparative isoelectric focusing, in particular).

10. Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jankovic et al (of record, J Immunol 135(2 suppl): 583s-587s, Aug 1985, PTO 892) in view of WO 97/13152 publication (or record, April 1997; PTO 1449), Ovary *et al* (Adv Biol Skin 11: 103-21, 1971; PTO 892), and Rotman *et al* (Prog Neuropsychopharmacol Biol Psychiatry 7(2-3): 135-41, 1983; PTO 1449).

Jankovic *et al* teach a diagnostic method for determining schizophrenia in a subject by detecting a delayed type hypersensitivity reaction to a human brain antigen such as brain S-100 protein and the high incidence of positive skin DTH reaction to the reference protein in schizophrenia indicates that cell-mediated immune processes may be involved in schizophrenia (See abstract, in particular).

The claimed invention in claim 6 differs from the teachings of the reference only in that the method for preparation of a reagent for use in diagnosis of schizophrenia in an individual by detecting a DTH reaction wherein the method step comprise obtaining blood sample from a number of individuals, preparing platelets therefrom, preparing a protein fraction from platelet having a pI greater than about 6.5 instead of neurospecific proteins S-100 and 10-40-4.

The claimed invention in claims 7-9 differs from the teachings of the reference only in that a diagnostic method for determining schizophrenia wherein the protein is platelet derived proteins or fractions thereof having a pI greater than about 6.5 instead of neurospecific proteins S-100 and 10-40-4.

The claimed invention in claims 10-13 differs from the teachings of the reference only in that a diagnostic method for determining schizophrenia wherein the protein is platelet derived proteins or fractions thereof having a pI within the range of about 6.5 to about 9.5 instead of neurospecific proteins S-100 and 10-40-4.

Deckmann *et al* teach autologous platelets elicit a skin reaction of delayed type hypersensitivity (DTH) reaction in patients with schizophrenia but not in normal subjects as evidence on page 3, paragraph 4 of instant specification.

The WO 97/13152 publication teaches a method for preparing a reagent for diagnosis of mental disorder such as dementia comprising the steps of obtaining blood from a number of individuals or individual such as demented patients or healthy normal subjects, isolating platelet from the said blood samples (See entire document, page 8 in particular), preparing protein fractions from the reference platelet preparation having a pI between 7 and 9, which is *greater than about* 6.5 (See page 12, Fig 4, page 10, Preparative isoelectric focusing, in particular). The reference pI is also within the claimed range of above 6.5 to about 9.5 (see page 12, lines 20-21, Fig. 4, in particular).

Ovary *et al* teach that the principal reason for the use of skin as a tool to study immunological phenomena because of its convenience. Skin has been used for decades to study allergic and immunologic response because skin reactions are easy to produce and observe and in many cases can be extremely sensitive in demonstrating sensitization (See page 103, 1st paragraph, in particular).

Rotman *et al* teach blood platelets are a very good model for nerve endings, serotonin uptake and imipramine binding and the efficiency of various drugs such as antidepressants have been evaluated using blood platelets instead of synaptosomes (See abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the brain S-100 protein as taught by Jankovic *et al* for the platelet protein preparation having a pI greater than 6.5 or within the range of above 6.5 to about 9.5 prepared by the method as taught by WO 97/13152 publication for a method of diagnosing schizophrenia in an individual by detecting a DTH as taught by Jankovic *et al,* WO 97/13152 publication, Jankovic *et al,* Ovary *et al* and Rotman *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Jankovic *et al* teach schizophrenia can be diagnosis with skin DTH reaction (See abstract, in particular). Ovary *et al* teach that the principal reason for the use of skin as a tool to study immunological phenomena because of its convenience. Skin has been used for decades to study allergic and immunologic response because skin reactions are easy to produce and observe and in many cases can be extremely sensitive in demonstrating sensitization (See page 103, 1st paragraph, in particular). Rotman *et al* teach blood platelets are a very good model for nerve endings, serotonin uptake and imipramine binding and the efficiency of various drugs such as antidepressants have been evaluated using blood platelets instead of synaptosomes (See abstract, in particular). Platelet preparation having a pI between 7 and 9 can be easily prepared by the method as taught by the WO 97/13152 publication for various neurological disorders (See page 12, Fig 4, page 10, Preparative isoelectric focusing, in particular).

Applicants' arguments filed 10/21/04 have been fully considered but are not found persuasive.

Applicants' position is that none of the cited references teach or suggest that platelet proteins might be useful in an assay for schizophrenia.

In response, Jankovic *et al* teach schizophrenia can be diagnosis with skin DTH reaction (See abstract, in particular). Platelet preparation having a pI between 7 and 9 can be easily prepared by the method as taught by the WO 97/13152 publication for various neurological disorders (See page 12, Fig 4, page 10, Preparative isoelectric focusing, in particular). Rotman *et al* teach blood platelets are a very good model for nerve endings, serotonin uptake and imipramine binding and the efficiency of various drugs such as antidepressants have been evaluated using blood platelets instead of synaptosomes (See abstract, in particular). The motivation to combine the references can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message

may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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